Introduction

Trauma is the most common cause of death among young people in the United States and around the world ***(Cothren et al., 2007).***

In addition, injuries from accidental trauma worldwide leave over 45 million people each year with moderate to severe disability ***(WHO, 2010).***

Hemorrhage is the most common preventable cause of death in the setting of trauma ***(Curry et al., 2011).***

Trauma-related hypovolemia may be associated with flow alterations that are inadequate to fulfill the nutritive role of the circulation. Adequate volume therapy appears to be fundamental in the management of the trauma patient ***(Tisherman et al., 2010).***

Rapid volume repletion is indicated in patients with severe hypovolemia or hypovolemic shock. Delayed therapy can lead to ischemic injury and possibly to irreversible shock and multiorgan system failure ***(Teixeira et al., 2009).***

During recent decades, despite our increasing knowledge of the pathophysiology of hemorrhagic shock in trauma patients, the mortality rate continues to remain high ***(Haut et al., 2011).***

A lethal triad of hypothermia, coagulopathy, and acidosis has been described as the cause of morbidity and mortality in trauma. This damage is related to the amount of fluid given during resuscitation ***(Sihler et al., 2010).***

About one-third of trauma patients will develop a coagulopathy if their hemorrhage leads to multiple organ failure ***(Rossaint et al., 2010).***

A long debate has ensued over the optimal fluid resuscitation regimen. More recently, damage control resuscitation, a combination of permissive hypotension, hemostatic resuscitation and damage control surgery, has been introduced to treat severely traumatized patients in hemorrhagic shock ***(Hsu et al., 2011).***

Goals of treatment in trauma patients remain avoiding metabolic acidosis, hypothermia, treating coagulopathy and stabilizing the patient as soon as possible ***(Hall et al., 2015).***

The method of fluid resuscitation, rate of infusion, and the types of fluids used during the resuscitation are important factors impact morbidity and mortality and are important components of the initial resuscitation of traumatic shock patients ***(Miller et al., 2013).***

In this review, we summarise the evidence guiding the initial period of resuscitation *from* prehospital resuscitation period *to* transfer to intensive care or operating theatre, focusing on trauma in critically injured adults.

Aim of the Work

The aim of this work is ***to*** review the role of early fluid resuscitation in adult polytrauma patients in decreasing morbidity and mortality rates , ***and*** discuss different modalities of fluid management in polytrauma patients giving merits and demerits of each type showing recent protocols & guidelines in early fluid resuscitation in adult polytrauma patients.

Pathophysiology of Polytrauma and Hemorrhagic Shock

Trauma is the leading cause of death in the United States within the age range of one to forty five years, causing nearly six million deaths per year worldwide ***(WHO, 2010).***

Trauma associated tissue injury initiates an inflammatory response and activates the coagulation cascade. Activation of the immune system and the subsequent inflammatory response is absolutely necessary for healing and defense against pathogens; however, greater magnitude and longer duration as seen with the systemic inflammatory response syndrome (SIRS) is associated with worse outcomes ***(Desai et al., 2011).***

Imbalanced systemic inflammation is the cause of inflammatory complications ***(Nuytinck et al., 1998).***

Regulation of pro-inflammatory and anti-inflammatory processes is therefore especially important and has significant implications regarding coagulation and resuscitation and potential future therapies ***(Peng et al., 2013).***

Trauma patients frequently suffer from blood loss requiring fluid resuscitation to provide essential tissue perfusion. While under-resuscitation leads to tissue hypo-perfusion and prolonged inflammatory response, we also must recognize that fluid resuscitation creates inflammatory consequences of its own ***(Cotton et al., 2006).***

Post-traumatic inflammatory response

The activation of the immune system following trauma is important for protection and healing of damaged tissues. Following severe trauma, the human body responds primarily via activation of the innate immune system in a way that is incredibly similar to other causes of the Systemic Inflammatory Response Syndrome (SIRS) and sepsis ***(Tsukamoto et al., 2010).***

It was thought that the post-traumatic SIRS response was bacterial in origin. It is now considered mostly a sterile process ***(Matzinger et al., 2002).***

Recently, it has been shown that the inflammatory response is a synchronous combination of pro-inflammatory and anti-inflammatory processes evident soon after trauma has occurred ***(Xiao et al., 2011).***

Severe injuries are associated with a proportional increase in Interleukin-6 (IL-6) and subsequent responses from the adaptive and innate immune systems ***(Jawa et al., 2011).***

Although the greater responsibility for tissue defense and repair falls to the innate immune system, some interesting changes occur in the adaptive immune system including decreased T1:T2 ratios. This diminished adaptive immunity and relative immune-suppression may lead to secondary infections ***(MacConmara et al., 2006).***

Traumatic tissue damage causes intracellular mediators to be released into the extracellular space and circulation at much higher concentrations than typically occurs with programmed cell death ***(Zhang et al., 2010).***

If this immune response becomes imbalanced and widely systemic with pronounced cytokine amplification, many proceed to the systemic inflammatory response (SIRS), multi-organ failure (MOF) and death ***(Marik et al., 2012).***

Recent data indicate that the resolution of an acute inflammatory response is an active process. It is promoted by

anti-inflammatory and pro-resolution mediators such as lipoxins, resolvins, and protectins ***(Recchiuti et al., 2012).***

Relationship between the inflammatory response and coagulation cascade

Major hemorrhage and its resulting coagulation abnormalities are major concerns to all who care for the severely traumatized patient since severe hemorrhage is considered the largest single cause of death within this patient population during the first 24-48 hours after trauma ***(Kauvar et al., 2006).***

Post-traumatic inflammation and coagulation cascade are inter-related and interactive ***(Figure 1) (Esmon et al., 2011).***

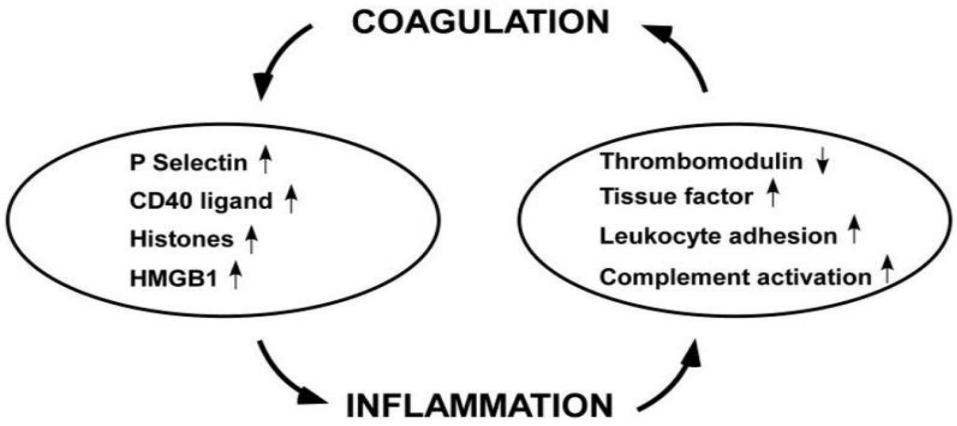

Fig. (1): The impact of coagulation on inflammation and the impact of inflammation on coagulation (Esmon et al., 2011).

Examples include histone-induced platelet activation, upregulation of plasminogen activator inhibitor (PAI), and down regulation of thrombomodulin, and histone-DNA complex triggering TLR-2, 4 and 9 activation with the end-result of increased inflammatory cytokine production ***(Semeraro et al., 2011).***

Inflammatory cytokines may also activate platelets and increase their expression of pro-coagulants ***(Levi et al., 2004).***

Coagulation factors activate the immune system as well. Formation of fibrin can trap bacteria and is associated with decreased bacterial dissemination ***(Degen et al., 2007).***

Also, activated platelets bind neutrophils, inducing formation of antimicrobial neutrophil DNA extracellular traps (NETs). Tissue factor-factor VIIa complex, thrombin, and factor Xa enhance the inflammatory response, while the naturally occurring anti-coagulants, such as activated protein C (aPC), help to limit this increased inflammation ***(Engelmann et al., 2013).***

Protein C has been shown to have anticoagulant and anti-inflammatory properties in response to trauma ***(Brohi et al., 2007).***

This newly described posttraumatic coagulopathy is associated with elevated plasma levels of activated protein C (aPC) and decreased protein C zymogen and is not due to dilution of coagulation factors caused by large fluid resuscitation ***(Christiaans et al., 2013).***

A complete blockade of the dual anticoagulant and anti-inflammatory properties of aPC led to much higher mortality rate, suggesting an important role for protein C in modulating inflammatory response and coagulation activation after severe trauma ***(Chesebro et al., 2009).***

For example, within the first six hours after trauma, increased plasma levels of circulating histones have been shown to be a predictor of mortality in trauma patients ***(Kutcher et al., 2012).***

Recent research in primates demonstrates that aPC may protect against excessive microvascular thrombosis by cleaving the pro-coagulant extracellular histones associated with endothelial dysfunction, organ failure, and death ***(Johansson et al., 2013).***

Thus, the massive activation of the protein C pathway after severe trauma appears to represent a maladaptive response of an important protective mechanism that prevents microvascular thrombosis and endothelial cell damage. Protection of the endothelium is important because endothelial integrity and homeostasis are critical for tissue perfusion, oxygenation and immune function ***(Chappell et al., 2009).***

In an attempt to break this vicious cycle, it is critical to provide adequate fluid resuscitation for perfusion of the microcirculation without increasing blood loss ***(Chappell et al., 2008).***

Relationship between inflammatory response and fluid resuscitation

Resuscitation of the severely traumatized patient has recently received a considerable amount of attention. A large volume crystalloid resuscitation, followed by several units of packed red blood cells then a modest amount of fresh frozen plasma and platelets was accepted as the standard for decades. This is no longer considered appropriate. Tissue damage from hypoperfusion is worsened by edema and linked to a systemic inflammatory response in a circular pattern ***(Figure 2). (Cohen et al., 2012).***

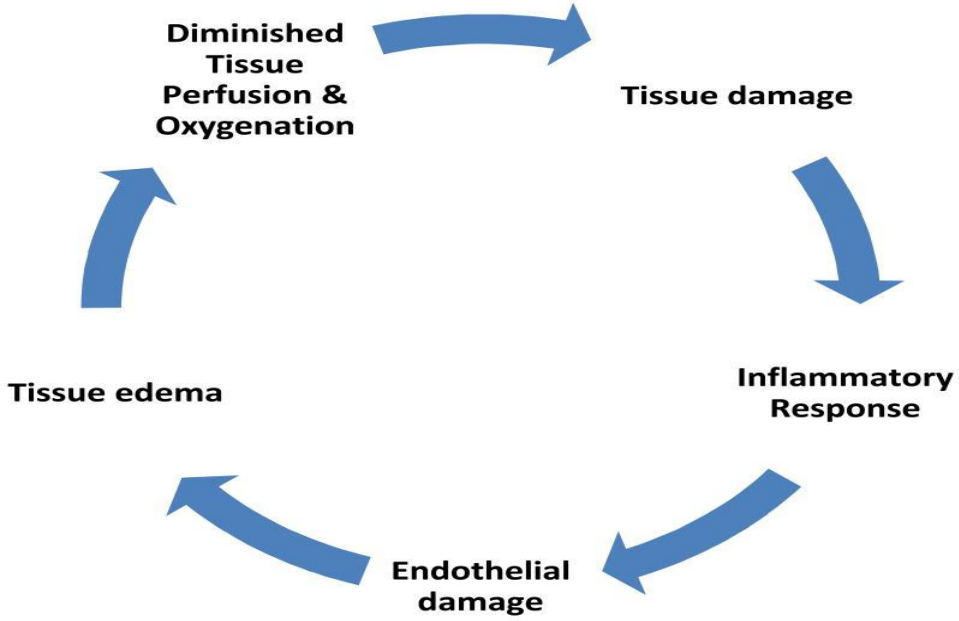

Fig. (2): The vicious cycle of tissue damage and inflammatory response (Cohen et al., 2012).

Tissue damage and shock leads to inflammation, which, if of a significant magnitude, leads to more tissue damage and shock ***(Neher et al., 2011).***

Current concepts of resuscitation are aimed at breaking this cycle thus allowing a more physiologic resolution of the inflammatory response, hopefully avoiding later detrimental sequelae ***(Chappell et al., 2008).***

Hypoperfusion of the microcirculation with traumatic shock causes the normal hemostasis of the vascular endothelium to be disrupted ***(Figure 3) (Tsukamoto et al., 2010).***

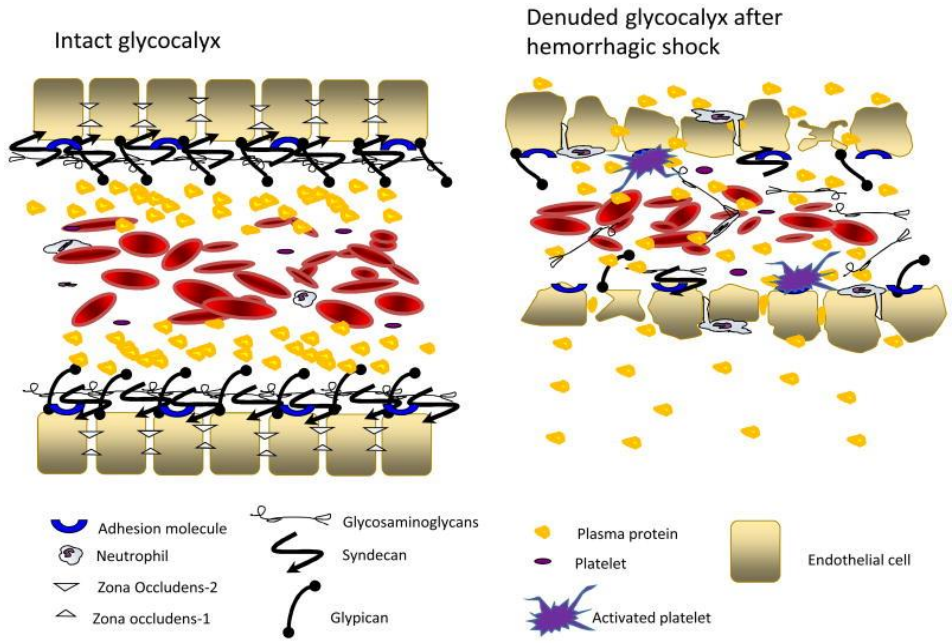

Fig. (3): Endothelial glycocalyx damage associated with systemic inflammation (Tsukamoto et al., 2010).

Loss of this glycocalyceal filtration along with disruption of the endothelial gap junctions allows the capillary leak that is typical of SIRS ***(Stein et al., 2012).***

Loss of intravascular proteins and volume to the tissue interstitium worsens tissue oxygenation and perfusion and is clinically evident as tissue edema ***(Chappell et al., 2009).***

However, an inflammatory response of sufficient magnitude may cause systemic glycocalyx degradation, endothelial cell swelling and apoptosis and widespread tissue edema with a resultant impairment of microperfusion and tissue oxygenation ***(Torres et al., 2013).***

The initial hypo-perfusion and tissue damage associated with shock initiate an inflammatory response that may be modulated by appropriate fluid resuscitation while minimizing blood loss from sites of uncontrolled bleeding, an approach described as damage control resuscitation (DCR) ***(Dutton et al., 2012).***

Two-hit theory of inflammatory response

The complex cascade of the host defense response is stimulated by primary and secondary insults (two hit theory) ***(Rotstein, 2003),***

❖ **First hits (primary insults):**

The trauma impact (trauma load) determines primaryorgan, or soft tissue, injuries and fractures with local tissuedamage as well as an activation of the systemic inflammatoryresponse ***(Napolitano et al., 2000).***

❖ **Second hits (secondary insults):**

In addition, secondary endogenous and exogenous factorsplay a crucial role in the initiation and severity of post traumaticcomplications ***(Waydhas et al., 1996).***

- **Typical endogenous (antigenic load) second hits are:**

✓ Respiratory distress with hypoxia.
✓ Repeated cardiovascular instability.
✓ Metabolic acidosis.
✓ Ischaemia/reperfusion injuries.
✓ Dead tissue.
✓ Contaminated catheters, or tubes.
✓ Infections. ***(Dunham et al., 1995)***